

HEWLETT-PACKARD COMPANY

Legal Department, 20BN
P.O. Box 10301
Palo Alto, California 94303-0890

PATENT APPLICATION **A**ATTORNEY DOCKET NO. 10980687-1

IN THE U.S. PATENT AND TRADEMARK OFFICE
Patent Application Transmittal Letter

ASSISTANT COMMISSIONER FOR PATENTS
Washington, D.C. 20231

Sir:

Transmitted herewith for filing under 37 CFR 1.53(b) is a(n): ☒ Utility () Design☒ original patent application,

() continuation-in-part application

INVENTOR(S): **Kenneth L. Staton et al.**TITLE: **HIGH QUANTUM EFFICIENCY POINT LIGHT DETECTOR**

Enclosed are:

☒ The Declaration and Power of Attorney. ☒ signed () unsigned or partially signed☒ 2 sheets of drawings (one set) () Associate Power of Attorney

() Form PTO-1449 () Information Disclosure Statement and Form PTO-1449

() Priority document(s) () (Other) _____ (fee \$ _____)

CLAIMS AS FILED BY OTHER THAN A SMALL ENTITY				
(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) TOTALS
TOTAL CLAIMS	8 — 20	0	X \$18	\$ 0
INDEPENDENT CLAIMS	1 — 3	0	X \$78	\$ 0
ANY MULTIPLE DEPENDENT CLAIMS	0		\$260	\$ 0
BASIC FEE: Design \$310.00); Utility \$760.00)				\$ 760
TOTAL FILING FEE				\$ 760
OTHER FEES				\$
TOTAL CHARGES TO DEPOSIT ACCOUNT				\$ 760

Charge \$ 760 to Deposit Account 08-2025. At any time during the pendency of this application, please charge any fees required or credit any over payment to Deposit Account 08-2025 pursuant to 37 CFR 1.25. Additionally please charge any fees to Deposit Account 08-2025 under 37 CFR 1.16, 1.17, 1.19, 1.20 and 1.21. A duplicate copy of this sheet is enclosed.

"Express Mail" label no. EL187272886USDate of Deposit October 7, 1999

I hereby certify that this is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

By Elizabeth MillerTyped Name: **Elizabeth Miller**

Respectfully submitted,

Kenneth L. Staton et al.By Bill Kennedy**Bill Kennedy**

Attorney/Agent for Applicant(s)

Reg. No. **33,407**Date: **October 7, 1999**Telephone No.: **(650) 857-4065**

HIGH QUANTUM EFFICIENCY POINT LIGHT DETECTOR

Field of the Invention

This invention relates to light detectors and more particularly to high quantum
5 efficiency point light detectors particularly adapted for detecting low levels of fluorescence.

Background

In many analytical situations, fluorescing molecules are attached to molecules of
interest to aid in their detection. Upon illumination, fluorescence indicates the presence of a
10 tagged moiety. The level of fluorescence is often quite low resulting in a low signal-to-noise
ratio.

In systems using a point detector such as a photomultiplier tube (PMT) the achieved
signal-to-noise ratio is often limited by the number of photons detected, i.e., by the number of
photons that result in the generation of a photoelectron in a photocathode that is subsequently
15 detected as a multi-electron pulse at the anode within the PMT. The ratio of the number of
electron pulses generated to the number of incident photons is called the quantum efficiency of
the detector. PMT's have a quantum efficiency that is significantly lower than one. Although
detectors that measure electric charges generated by incident radiation such as charge-coupled
devices (CCD's) are known to have a much higher quantum efficiency than PMT's, it has been
20 assumed that the PMT is the best solution available for use as a point detector. This was the
case because CCD's, though having higher quantum efficiency, suffer from dark current-related
electron shot noise and especially from readout noise.

In multi-pixel (imaging) situations with very long integration times such as in
astronomical photography the multiple readout of a CCD has been used. However, the
25 inventors herein are unaware of any prior art realization that a CCD can be modified into a
point detector that can outperform a PMT in terms of achieved signal-to-noise ratio.

Summary

The high quantum efficiency point detector system according to the invention includes a
30 light source generating a light beam having an area, and a detector for receiving the light beam,
the detector having a cell size comparable to the light beam area. The detector may be any
detector that measures electric charges generated by incident radiation such as a charge-coupled
device (CCD). The cell may have a single relatively large pixel or it may have an array of two
or more pixels. The system further includes a readout capacitor and apparatus for transferring,

multiple times, charge from the detector to the capacitor and back. It is preferred that a plurality of transfer and readout capacitors be provided for multiple readouts. Further, readout noise can be reduced by reading out a single CCD element multiple times and averaging the results.

5

Brief Description of the Drawings

Fig. 1 is a schematic view of a CCD array.

Fig. 2 is a schematic view of an optical fiber-CCD combination.

Fig. 3 is a schematic diagram illustrating a pipeline arrangement of readout capacitors.

10

Fig. 4 is a schematic diagram illustrating a cyclic arrangement of readout capacitors.

Description of the Preferred Embodiment

With reference to Fig. 1 a detector such as a CCD array 10 in this embodiment is made up of 25 pixels each pixel approximately 10 μ m square. Thus, the overall cell size is 50 μ m.

15

The cell size of the CCD array 10 could be as large as desirable for ease of alignment with a light source without increasing dark current to unacceptable levels. The array in Fig. 1 is entirely exemplary and a CCD may have only a single large cell or fewer than the 25 pixels illustrated in Fig. 1.

20

As an example of the invention, a light source (e.g., the focal spot of a confocal scanner or the end of a fiber) might be imaged onto a single pixel of a CCD array, onto a small number of adjacent pixels of a CCD array or onto a custom made, single pixel CCD. With reference to Fig. 2, an optical fiber 12 is brought almost into contact with the CCD array 10. The CCD 10 will offer higher quantum efficiency than a PMT especially in the (infra) red spectral region and especially for a backthinned and back illuminated CCD. It should be noted that light from the fiber 12 may be imaged onto the array 10.

25

In operation, the CCD 10 collects light during the duration of a light collection period sometimes referred to as a pixel. After that period, its charge is transferred to a readout capacitor and the voltage across that capacitor can then be sampled. As there is finite transfer noise, multiple transfers result in different numbers of electrons in the readout capacitor and thus in different voltages. By transferring the charge into and out of the readout capacitor multiple times and by averaging the readings, one can diminish the impact of this readout noise by a significant amount.

30

If the maximum readout frequency is too low to do the multiple readouts within the duration of a single pixel, it is contemplated to build a chip with multiple transfer and readout

capacitors. A given pixel charge would then be passed onto a given transfer capacitor and would be bounced back and forth between that capacitor and its readout capacitor for multiple readouts. Meanwhile, the next pixel charge could be passed into the next transfer capacitor and so on, until a cyclic repetition occurs. The number of transfer/readout capacitor pairs will be the smallest integer that is not smaller than the readout/averaging time divided by the pixel time. The readout/averaging time is the total time the charge spends passing through the readout capacitor's circuitry. The time for an individual measurement of the charge in one of the capacitors will be shorter. Many measurements may be averaged.

If multiple capacitors are used for charge to be stored in and read out from while subsequent charge collection processes are in progress, these capacitors may be arranged in a pipeline fashion as shown in Fig. 3. A first charge is generated in a light-sensitive area 30 and then moved to a first capacitor/readout unit 31. While a second charge is generated in the light-sensitive area 30, the first charge is read out and cycled back as often as desired. Once the second charge has been generated, the first charge is either dumped or moved into a second capacitor/readout unit 32, while the second charge is moved to the first capacitor 31 after which a third charge can be generated in the photo-sensitive area 30. All readings of a given charge taken from different capacitors are averaged to reduce the noise on the charge measurement. This process can be extended in a similar fashion to a large number of capacitors (32 through 33), thus reducing read-out noise. In this design, any given charge is essentially moved along a line of capacitors to allow it to be read out as often as desired. After all desired readout/averaging is done, the charge is dumped (as in a conventional CCD).

In an alternate design shown in Fig. 4, there are several (in this case four) capacitors with associated readout circuitry arranged around the light-sensitive area 30. Charge from individual charge generation cycles (pixel times) is transferred to these capacitors, e.g., cycling around: A first charge is moved to capacitor/readout unit 35 and stays there for four pixel cycles for repeated readout. One pixel cycle later the next charge is moved to capacitor/readout unit 36, another cycle later the next charge is moved to capacitor/readout unit 37. The next charge generated is moved to capacitor/readout unit 38. Once the next charge is generated, the charge in capacitor/readout unit 35 is dumped and the new charge is moved there, thus restarting the cyclic acquisition of data.

The readout values can be accumulated using known methods (e.g., analog-to-digital conversion of resulting voltages and subsequent (weighted) averaging) in a control unit 34.

The impact of dark current and the electron shot noise accompanying it can be minimized either by cooling the CCD or by increasing the photon rate to the point in which the resulting photocurrent exceeds the dark current.

In a specific design the single readout noise might be eight electrons, the pixel time
5 10 μ s and the readout time 1 μ s; this will result in an effective readout noise of less than three
electrons. The higher quantum efficiency of the single large cell CCD of the invention coupled
with the fact that PMT's have excess noise unless used in a photon counting mode (which, if
used, limits dynamic range) results in better overall performance than a PMT-based detection
scheme. In addition, the invention allows easy integration of multiple detectors on a single die,
10 resulting in significant cost savings in a system that, for example, is used to detect more than
one (spectral) channel at a time. The invention thus provides a detection scheme that has higher
quantum efficiency than a PMT while reducing readout noise and dark current electron shot
noise of CCDs.

It is recognized that modifications and variations of the invention will occur to those
15 skilled in the art and it is intended that all such modifications and variations be included within
the scope of the appended claims.

Claims

What is claimed is:

1. High quantum efficiency point detector system comprising:
a light source generating a light beam having an area; and
a detector with a cell size comparable to light beam area.
2. The detector system of claim 1 wherein the cell includes a single pixel.
3. The detector system of claim 1 wherein the cell includes at least two pixels.
4. The detector system of claim 1 further including a readout capacitor and means for transferring, multiple times, charge from the detector to the capacitor.
5. The detector system of claim 1 further including a plurality of transfer and readout capacitors.
6. The system of claim 1 wherein the detector is a CCD detector.
7. The detector system of claim 5 wherein the plurality of transfer and readout capacitors are arranged in a pipeline configuration.
8. The detector system of claim 5 wherein the plurality of transfer and readout capacitors are arranged in a cyclic pattern around a light sensitive area.

High quantum efficiency point detector system. The system includes a light source generating a light beam having an area and includes a CCD detector with a cell size comparable to the light beam area. The CCD cell may include a single pixel or at least two pixels.

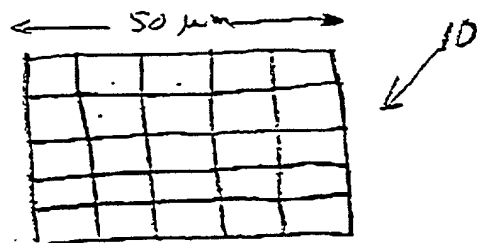


FIG. 1

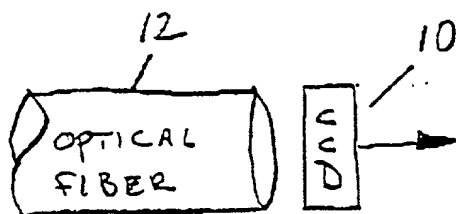


FIG. 2

09415015-100399

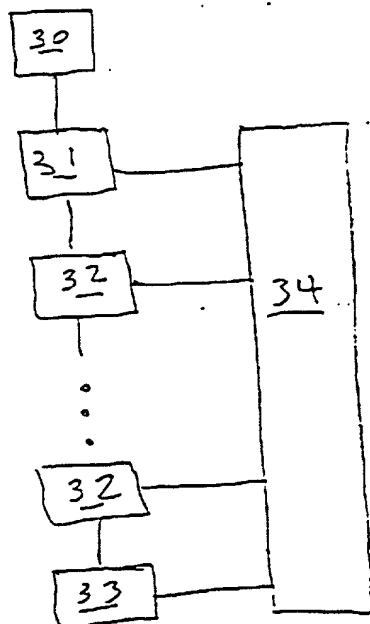


FIG. 3

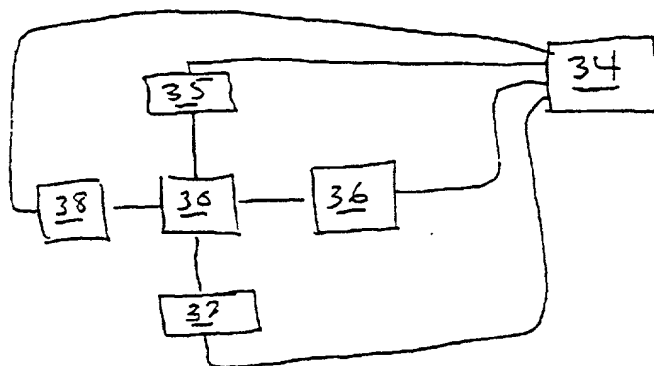


FIG. 4

**DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION**ATTORNEY DOCKET NO. 10980687-1

As a below named inventor, I hereby declare that:

My residence/post office address and citizenship are as stated below next to my name;

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

HIGH QUANTUM EFFICIENCY POINT LIGHT DETECTOR

the specification of which is attached hereto unless the following box is checked:

() was filed on _____ as US Application Serial No. or PCT International Application Number _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understood the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose all information which is material to patentability as defined in 37 CFR 1.56.

Foreign Application(s) and/or Claim of Foreign Priority

I hereby claim foreign priority benefits under Title 35, United States Code Section 119 of any foreign application(s) for patent or inventor(s) certificate listed below and have also identified below any foreign application for patent or inventor(s) certificate having a filing date before that of the application on which priority is claimed:

COUNTRY	APPLICATION NUMBER	DATE FILED	PRIORITY CLAIMED UNDER 35 U.S.C. 119
			YES: _____ NO: _____
			YES: _____ NO: _____

Provisional Application

I hereby claim the benefit under Title 35, United States Code Section 119(e) of any United States provisional application(s) listed below:

APPLICATION SERIAL NUMBER	FILING DATE

U. S. Priority Claim

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NUMBER	FILING DATE	STATUS (patented/pending/abandoned)

POWER OF ATTORNEY:

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) listed below to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

Bill Kennedy**Gordon Stewart****Philip S. Yip****Herbert R. Schulze**Reg. No. **33,407**Reg. No. **30,528**Reg. No. **37,265**Reg. No. **30,682**

Send Correspondence to:
IP Administration
Legal Department, 208N
HEWLETT-PACKARD COMPANY
P.O. Box 10301
Palo Alto, California 94303-0890

Direct Telephone Calls To:

Bill Kennedy
(650) 857-4065

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of Inventor: **Kenneth L. Staton**Citizenship: **US**Residence: **574 Wellington Drive, San Carlos, CA 94070**Post Office Address: **Same as residence**

Kenneth L. Staton
Inventor's Signature

10/7/99
Date


**DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION (continued)**

ATTORNEY DOCKET NO. 10980687-1

Full Name of # 2 joint inventor: Andreas N. Dorsel Citizenship: DE

Residence: 140 Santa Margarita Avenue, Menlo Park, CA 94025

Post Office Address: Same as residence

 10/07/99
Inventor's Signature Date

Full Name of # 3 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date

Full Name of # 4 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date

Full Name of # 5 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date

Full Name of # 6 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date

Full Name of # 7 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date

Full Name of # 8 joint inventor: _____ Citizenship: _____

Residence: _____

Post Office Address: _____

Inventor's Signature Date